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iii) separating the protein extracts; and

iv) detecting protein alkylation of the protein extracts by measuring microtubule depolymerization and formation of modified  $\beta$ -tubulin.

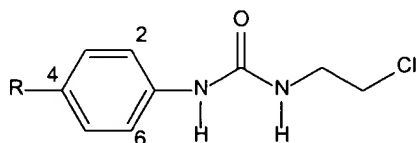
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### REMARKS

By the subject Amendment Applicants have amended the Specification, cancelled Claim 4 without prejudice and added Claim 8. Accordingly, Claims 1 to 3 and 5 to 8 are pending herein. Claims 1 and 8 are presented in independent form. Claims 1 to 3 and 5 to 7 have been withdrawn from consideration by the Examiner. Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The Specification beginning at page 3 (line 22) was amended by the insertion of the following paragraph:

-- In accordance with the present invention, there is also provided a method for detecting protein alkylation achieved by a compound of formula I, or a pharmaceutically acceptable salt thereof:



formula I

wherein R is selected from the group consisting of *t*-butyl, *i*-propyl and *s*-butyl. The method involves incubating a human carcinoma cell line with the compound of formula I, to provide incubated cells; harvesting the incubated cells to obtain protein extracts; separating the protein extracts;

and detecting protein alkylation of the protein extracts by measuring microtubule depolymerization and formation of modified  $\beta$ -tubulin. –

Support for this amendment can be found on pages 12-18 as well as in Claim 4 of the Specification as originally filed.

The Specification was objected to by the Examiner pursuant to 37 CFR 1.75(d)(1) for allegedly failing to provide proper antecedent basis for the claimed subject matter. More specifically, the Examiner alleged that the subject matter as defined by Claim 4 (as originally filed) is not supported by the Specification. Applicants have cancelled Claim 4 without prejudice and added new Claim 8 to the Specification. Applicants respectfully submit that this amendment is permissible since the subject matter of Claim 8 (new) was part of the Specification as originally filed. Furthermore, Applicants have amended the disclosure by incorporating therein Claim 8 (new).

Claim 4 was rejected by the Examiner under 35 U.S.C. 112, first paragraph, as allegedly based on a non-enabling disclosure. Applicants have cancelled Claim 4 without prejudice and have added new Claim 8 to the Specification. Applicants respectfully submit that Claim 8 (new) is fully supported by the disclosure as originally filed.

Claim 4 is rejected by the Examiner under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard to be the invention. Claim 4 has also been rejected by the Examiner under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements. Applicants respectfully submit that because Claim 4 has been cancelled and Claim 8 (new) fully complies with 35 U.S.C. 112, second paragraph, the Examiner's prior rejection is rendered moot. Claim 8

distinctly claims a method for detecting protein alkylation brought about by the compounds of the present application and is fully supported by the disclosure as originally filed.

No new subject matter has been added to the claims. The amendments to the claims are fully supported by the Specification as originally filed.


A marked up version showing amendments to the Specification and claims is provided in the attached "Marked up Version of Amendments." Changes are shown using underlines and strikeouts.

### CONCLUSION

In view of the cancellation of Claim 4 without prejudice and the addition of new Claim 8 and of the mostly editorial changes to the disclosure, the present application is believed to be in condition for allowance and a notification to this effect is requested. It is believed that no fee is due for this submission. Should that determination be incorrect, however, the Examiner is hereby authorized to charge any deficiencies to our Deposit Account No. 13-2759, and notify the undersigned in due course. Should the Examiner have any questions or wish to discuss further this matter, please contact the undersigned at the telephone number provided below.

Date: 1/22/03

Respectfully submitted,

  
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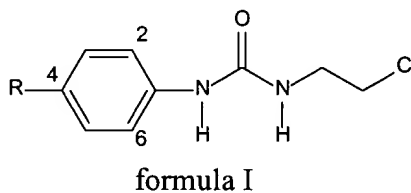
## MARKED UP VERSION OF AMENDMENTS

### Specification Amendment

The specification and claims have been amended as follows. Underlines indicate insertions and ~~strikeouts~~ indicate deletions.

At page 3, the following paragraph was added:

-- In accordance with the present invention, there is also provided a method for detecting protein alkylation achieved by a compound of formula I, or a pharmaceutically acceptable salt thereof: process:

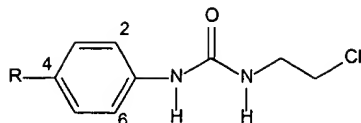


wherein R is selected from the group consisting of *t*-butyl, *i*-propyl and *s*-butyl. The method involves incubating a human carcinoma cell line with the compound of formula I, to provide incubated cells; harvesting the incubated cells to obtain protein extracts; separating the protein extracts; and detecting protein alkylation of the protein extracts by measuring microtubule depolymerization and formation of modified  $\beta$ -tubulin. --

### Claim Amendments

Claim 4 has been cancelled without prejudice and Claim 8 has been added as follows:

8. (New) A method for detecting protein alkylation achieved by a compound of formula I, or a pharmaceutically acceptable salt thereof:



formula I

wherein R is selected from the group consisting of *t*-butyl, *i*-propyl and *s*-butyl, comprising the method steps of:

- v) incubating a human carcinoma cell line with the compound of formula I, to provide incubated cells;
- vi) harvesting the incubated cells to obtain protein extracts;
- vii) separating the protein extracts; and
- viii) detecting protein alkylation of the protein extracts by measuring microtubule depolymerization and formation of modified  $\beta$ -tubulin.